

### REMARKS/ARGUMENTS

This Amendment incorporates the amendments to the claims contained in the Amendment After Final Rejection filed May 1, 2009. The Remarks included in the May 1 Amendment are incorporated herein by reference.

#### Evidence of Record

It is not clear whether the evidentiary Declaration made April 7, 2009 by Dr. New has been entered. Entry and consideration of same are hereby requested.

Also submitted with this Amendment is a further Evidentiary Declaration of Dr. New made July 31, 2009 addressing comments included in the Official Action of August 5, 2008. This evidence confirms that adding acid to reduce the pH of a solution in accordance with US '748 leads to precipitation of around pH 6.7.

#### Amendments to the Claims / New Claims

Claims 1 and 26 are above amended to specify the composition does not raise the pH of the intestinal fluid to above pH 7.0, as previously featured in claims 34 and 35, now canceled.

Claims 1 and 26 are also amended to specify the compositions are solids. Basis for the reference to a solid composition may be found throughout the description e.g. at page 9, lines 17 to 18.

New dependent claims 39 and 40 specify the compositions of claims 1 and 26 respectively comprise at least 66 mg of bile acid or salt is to be used. The four *in vivo* Examples in this case (Examples 6 to 9) all feature 66 mg of bile acid or salt, and so provide support for the limitation in the minimum amount of bile acid or salt.

New dependent claims 41 and 42 have been added based on the description on page 7, lines 10-14 of the specification.

#### Response to Examiner's Comments

Applicant now specifically addresses the issues presented and comments made in the Advisory Action.

The Advisory Action of June 8, 2009 contains essentially two objections. The first is to the reference to "analogues" and "derivatives" in claims 9-11 and 19-21. The second is an obviousness objection, which applies to all of the claims.

### **Objection to claims 9-11 and 19-21**

The Examiner's objections imply that the efficacy or success of the combined formulation depends closely on the exact sequence of the peptides/proteins being used according to the present invention. However, this is not the case. As explained at page 1 lines 13-19 of the present application as filed, the mechanism by which the bile salts and acids operate according to the present invention is believed to involve the transient opening of large water channels such as tight junctions, through which active principles can diffuse. Clearly, the ability to diffuse is unrelated to the chemical nature of the peptide incorporated, and this is demonstrated by the examples presented, which show that uptake can occur for different macromolecules which bear no resemblance to each other - insulin and salmon calcitonin. It is therefore reasonable to suppose that any other macromolecule would be taken up just as easily, regardless of e.g. its amino acid sequence in the case of peptides. On this basis, it is respectfully submitted that the Examiner's objections are not well-founded, and so should be withdrawn.

### **Obviousness objection**

Previously the Examiner has taken the position that the pH of the '748 compositions could easily be reduced to below 7.5, despite the Applicant's arguments that this would require sufficiently large quantities of acid to be impractical. Claims 1 and 26 have now been amended to require the presence of a minimum of 60 mg of the bile acid or salt for use according to the invention. Accordingly, the amount of acid that would now be required in order to reduce the pH of the relevant composition from 8-8.5 down to 6.8-7.5 (see the last sentence of the last full paragraph on page 2 of the Advisory Action) is now significantly higher, to the extent that it really would be unfeasible to reduce the pH in the manner suggested by the Examiner. Accordingly, it is respectfully submitted that the Examiner's obviousness objection, which is based on the notion that it would be obvious to add aromatic alcohols to the bicarbonate-containing compositions of US 5,853,748 and then to reduce their pH, should be withdrawn.

Regarding the Examiner's comments in respect of the Declaration made April 7, 2009, it should be noted that the claims are now directed to solid formulations.

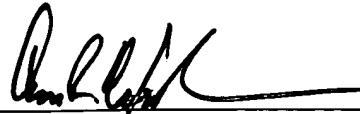
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Appl. No. 10/553,169  
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Favorable reconsideration of this application is respectfully requested.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_



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